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## FUNCTIONAL CHANGES IN THE GASTRIC GLANDULAR APPARATUS IN SECRETORY ACTIVITY OF LONG DURATION

Fiziologiya nervnykh protsessov [Physiology of Nerve Processes], 1955, Kiev, Pages 396-404

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One of the major directions in the research of professor Georgii Vladimirovich Fol'bort, member of the Academy of Sciences Ukrainian SSR is the study of the processes of functional exhaustion and recovery of working organs.

The foundation for these researches was laid in the works of the great Russian physiologist, Ivan Petrovich Pavlov, in 1890 in his studies of the material substrate of physiological processes. Pavlov showed that stimulation of the salivary gland results in two mutually contradictory processes: the destruction and the restoration of the substances of cellular protoplasm. Both processes occur while the organ is active and also while it is at rest; but in the former state the process of destruction, exhausting the working tissue, is more pronounced, while during rest the process of recovery, acccompanied by accumulation of the substances of cell protoplasm, is dominant.

While still working in Pavlov's laboratory, Fol'bort showed in 1917 that the principles of the processes of exhaustion and recovery established by Pavlov in acute experiment could also be demonstrated in chronic experiment by the method of intermittent feeding developed by collaborators by Pavlov. The essence of the method is found in the fact that repeated feeding of small quantities of food to an animal produces an additive effect in food stimulus and intensified glandular activity, resulting in a reduction in the work-capability of the glandular tissue.

In experiments involving virtually all the major digestive glands, in 1932 A. B. Fel'dman, and in 1940 E. I. Aleksentseva, N. K. Zol'nikova, M. P. Kovalenko, E. N. Gofman, and other collaborators of G. V. Fol'bort, followed by Ya. P. Sklyarov with salivary gland studies in 1948, and his associates Z. V. Dovgan' in 1952, P. T. Karavayev, A. P. Grechishkin, and V. S. Savron in 1954, and A. G. Kantser on gastric glands in 1935, and M. P. Nikiforovskaya and I. V. Shostakovskaya on the pancreas in 1954, investigated the major laws involved in the processes of exhaustion and recovery of working glandular tissue. The major indic... thereof were the changes in the changes in the chemical composition of the substances thus secreted.

E. D. Bromberg, in his study of the salivary glands, and A. G. Kantser, studying the pancreas, have attempted to investigate the chemical changes in glandular tissue in chronic experiment. Although the methods employed more nearly resembled those of semiacute experiments, these workers were able to shed light on one of the aspects of functional change in glandular tissue.

In our own laboratory V. S. Savron' and L. N. Karpenko developed in 1954 an entirely satisfactory method of simultaneous study of structural and chemical changes in the gastric mucosa, the secretory process and the chemical composition of gastric juice. Some of the researches thus performed have already been published, while the present communication sets forth new data.

Excision of the mucosa is performed under visual control, via a fistula in the larger or smaller curvature. The canine subjects of experiment reveal no pain when this is done, the course of the process of secretion is not affected, and minor loss of blood ceases within 5 to 10 minutes after excision for which a special instrument is used.

Let us examine, to begin with, the morphological changes in glandular cells after secretion of long duration (Figure 1, microphoto). The reproduction shows the state of the mucosal cells before the start of long-lasting secretory activity (slide by V. S. Savron'). The major cells contain many secretory granules, the nuclei are quite clear, and the cell borders are delineated distinctly. The cells lining the stomach are so solidly packed with secreting granules that the nuclei are completely invisible.

The condition of the gastric mucosa after long-term secretion, shown in Figure 2, is entirely different. The major cells are empty, containing virtually no granules of secretion, and the borders of the cells are blur-red at many points. The stomach-lining cells have also lost a considerable portion of their granules of secretion. In many cases, a light-colored border appears around the nuclei of the lining cells, while the periphery of the cell continues to show granular structure.

Comparison of our observations with those of other workers (Heidenhain, 1870; Nol' and Sokolov, 1906; Lasovskiy, 1938) shows that all these had reported disappearance of the granular structure of the cells after secretion. However, Nol' and Sokolov reported that in the lining cells, the granular structure was restored so quickly during secretion that it was impossible to identify the changes therein. Our observations also showed morphological changes in the cells to be insignificant when secretion was for short periods. But subsequent to long periods of secretion there were unmistakable changes in internal cell structure.

TABLE 1

CHANGES IN THE COMPOSITION OF GASTRIC MUCOSA AND GASTRIC JUICE SUBSEQUENT TO LONG PERIODS OF SECRETION BY THE GLANDS OF THE STOMACH

Dog Tresor, 11.2 kg in weight

| Time | Stimulus | Latent period, minutes | Juice secreted, quantity | Digestive strength of juice, mm | Chlorides, quantity | Residual solids (%) | Residual ash (%) | Organic residue (%) |
|---|---|---|---|---|---|---|---|---|
| Experiment of 21 January 1954 | | | | | | | | |
| [1] | [2] | [3] | [4] | [5] | [6] | [7] | [8] | [9] |
| | Mucosa | | | 15.5 | 591.6 | 20.7 | 1.5 | 19.2 |
| 0945 | Bread 60.0 | | | | | | | |
| 1045 | | 5 | 3.5 | 5.0 | 439.75 | 2.9 | 0.8 | 2.1 |
| 1145 | | | 3.0 | 5.0 | 514.75 | 3.0 | 0.7 | 2.3 |
| 1245 | | | 3.0 | 5.2 | 426.0 | | | |
| 1345 | | | 4.0 | 4.6 | 497.0 | | | |
| 1445 | Bread 60.0 | | 4.0 | 4.0 | 439.75 | | | |
| | Water 50.0 | | | | | | | |
| 1545 | | | 4.0 | 5.0 | 439.75 | | | |
| 1645 | | | 3.5 | 4.2 | 439.75 | | | |
| 1745 | | | 3.0 | 3.6 | 428.0 | | | |
| 1845 | | | 2.5 | 3.0 | 426.0 | | | |
| 1945 | | | 3.0 | 3.2 | 408.25 | | | |
| 2045 | | | 3.0 | 2.4 | 439.75 | 1.6 | 0.7 | 0.9 |
| 2145 | | | 3.0 | 2.0 | 426.0 | 1.7 | 0.9 | 0.8 |
| | Mucosa | | | 13.0 | 517.8 | 18.8 | 1.6 | 17.2 |

**Experiment of 22 January 1954**

| [1] | [2] | [3] | [4] | [5] | [6] | [7] | [8] | [9] |
|---|---|---|---|---|---|---|---|---|
| | Mucosa | | | 15.0 | 458.5 | 20.6 | 1.6 | 19.0 |
| 1030 | Bread 200.0 | 5 | | | | | | |
| 1130 | | | 5.0 | 3.6 | 439.75 | 2.0 | 0.6 | 1.4 |
| 1230 | | | 4.5 | 3.0 | 426.0 | | | |
| 1330 | | | 2.0 | 3.2 | 426.0 | | | |
| 1430 | | | 0.5 | - | - | | | |
| | Mucosa | | | 14.5 | 475.6 | 20.5 | 1.5 | 19.0 |

**Experiment of 23 January 1954**

| [1] | [2] | [3] | [4] | [5] | [6] | [7] | [8] | [9] |
|---|---|---|---|---|---|---|---|---|
| | Mucosa | | | 17.0 | 550.7 | 22.0 | 1.7 | 20.3 |
| 0930 | Bread 200.0 | | | | | | | |
| 1030 | | 4 | 4.5 | 4.0 | 496.0 | 2.0 | 0.8 | 1.2 |
| 1130 | | | 4.0 | 3.8 | 496.0 | | | |
| 1230 | | | 3.0 | 3.8 | 462.0 | | | |
| 1330 | | | 1.0 | - | - | | | |
| | Mucosa | | | 16.5 | 517.5 | 22.1 | 1.6 | 20.5 |

**Experiment of 24 January 1954**

| [1] | [2] | [3] | [4] | [5] | [6] | [7] | [8] | [9] |
|---|---|---|---|---|---|---|---|---|
| | Mucosa | | | 15.5 | 518.75 | 20.8 | 1.5 | 19.3 |
| 0930 | Bread 200.0 | | | | | | | |
| 1030 | | 4 | 5.5 | 4.6 | 408.25 | 2.6 | 0.8 | 1.8 |
| 1130 | | | 4.0 | 4.4 | 426.0 | | | |
| 1230 | | | 2.5 | 4.4 | 408.25 | | | |
| 1330 | | | 1.0 | - | | | | |
| | Mucosa | | | 15.0 | 575.0 | 20.2 | 1.3 | 18.9 |

**Experiment of 25 January 1954**

| [1] | [2] | [3] | [4] | [5] | [6] | [7] | [8] | [9] |
|---|---|---|---|---|---|---|---|---|
| | Mucosa | | | 15.0 | 548.5 | 21.0 | 1.4 | 19.6 |
| 1020 | Bread 200.0 | | | | | | | |
| 1120 | | | 5.0 | 5.8 | 479.25 | 3.1 | 0.9 | 2.2 |

| [1] | [2] | [3] | [4] | [5] | [6] | [7] | [8] | [9] |
|---|---|---|---|---|---|---|---|---|
| [illegible] | | | 2.5 | 5.4 | [illegible] | | | |
| 1320 | | | 2.5 | 5.6 | 462.0 | | | |
| 1420 | | | 0.5 | - | - | | | |
| | Mucosa | | | 15.5 | 537.2 | 20.9 | 1.5 | 19.4 |
| | **Experiment of 26 January 1954** | | | | | | | |
| 0930 | Mucosa<br>Bread 200 | | | 14.5 | 585.8 | 21.2 | 1.4 | 19.8 |
| 1030 | | 3 | 4.0 | 5.0 | 497.0 | 2.8 | 0.7 | 2.1 |
| 1130 | | | 3.5 | 5.2 | 426.0 | | | |
| 1230 | | | 3.5 | 4.8 | 462.0 | | | |
| 1330 | | | 2.0 | 4.8 | 497.0 | | | |
| 1430 | | | 0.5 | - | - | | | |
| | Mucosa | | | 14.0 | 518.25 | 21.3 | 1.5 | 19.8 |

Study of the chemical changes in the gastric mucosa resulted in the discovery of exceedingly interesting phenomena. Table 1 presents data from the experiments of L. N. Karpenko on changes in the composition of the gastric mucosa and the gastric juice subsequent to long periods of secretion by the gastric glands (12-hour experiment), and also shows how the composition of the gastric juice and mucosa changed during the following days.

As is evident from the data, the secretion of juice throughout almost the entire day of the experiment remained virtually unchanged; neither did the rate of secretion show any significant changes. The peptic activity, which was 5 mm on the Mett scale at the beginning of the activity, dropped to 2 mm at the end of a long experiment. This testifies to the fact that the concentration of ferment in the juice declined from 25 to 4 units, or by more than 5/6.

Marked changes also occurred in the solid residue of the gastric juice. While, at the outset of an experiment of long duration it was 2.9 to 3.0%, at the end it dropped to 1.6-1.7%, i.e., the concentration of solids in the juice dropped by more than half. The decline in the solid residue was due to reduction by more than half in the organic substances in the juice, while the absolute content of organic materials remained virtually unchanged. Despite the marked fluctuation in the quantity of chlorides in the composition of the gastric juice, it remained virtually the same toward the end of the experiment.

In experiments of long duration there was considerable change in the composition of the gastric mucosa before and after secretion. Before secretion, the peptic activity was 15.5 mm on the Mett scale, but after a long period of secretion it dropped to 13 mm. In accordance therewith, and with Borisov's Law (1891), concentration of ferment in the mucosa dropped from 240.25 to 169.0 units. In addition, the solid residue and chlorides in the gastric mucosa dropped as a result of the decline in its organic component.

Thus, long-continued gastric-gland activity led not only to changes in the chemical composition of the juice, but to change in the chemical composition of the mucosa, in particular of those components which are excreted in the gastric juice. This is direct confirmation of the ideas repeatedly expressed by Pavlov as to the consumption of matter during tissue activity, and on the consequent decline in the efficiency of the various organs. These experiments confirm the data on functional exhaustion derived by G. V. Fol'bort and his associates.

The profundity of the changes in the gastric mucosa is less marked than that of the changes in the composition of the gastric juice. This testifies to the fact that it is not only the consumption [illegible] is significant in functional exhaustion, but the weakening of the mechanisms by means of which gastric secretion takes place.

The example at hand provides renewed confirmation for Pavlov's observation as to the significance of "damage to the mechanisms" in the phenomena of functional exhaustion, this being the phenomenon responsible for actuating the apparatus of gastric secretion (I. P. Pavlov, 1890).

Study of the process of recovery of the chemical composition of the gastric juice demonstrates that peptic activity, and the solid residues of the juice attain their initial magnitudes only on the third day subsequent to an experiment of long duration. After attaining its initial value, the peptic activity of the juice then rises above that level, declining to that point again only on subsequent days. Analogous changes are undergone by the organic substances of the solid residue and the chlorides. However, one must note that change in the chloride content is subject to less severe laws than, for example, change in the peptic activity of the juice. In the majority of experiments, there is no significant change in the quantity of chlorides.

Restoration of the composition of the gastric mucosa proceeds considerably faster than that of the chemical composition of gastric juice. On the second day of restoration, the peptic activity of the mucosa and the amount of solid residue in the mucosa is greater than in the initial experiment. Subsequently, the composition of the mucosa returns to magnitudes of the previous order.

The difference in the rate of recovery of the composition of the gastric mucosa and of the chemical composition of the juice it secretes testifies to the fact that, in addition to the recovery occurring in the mucosa, high significance is ascribable to the restoration of the efficiency of the mechanisms by which gastric secretion is stimulated.

To clarify this question, experiments were set up to illustrate the role of nervous stimuli in the processes of recovery. We did not give major attention to the role of chemical influences on the gastric glands, as our prior studies had demonstrated that chemical stimuli such as histamine have but a weak effect on the trophic activity of the gastric glands. In dogs whose vagus nerves had been exteriorized and shredded, and which had gastric fistulas, this nerve was stimulated by a current of induction. Secretion accompanying this was completely insignificant, but the mucosa showed marked changes in composition. Table 2 presents the results of one such experiment.

As may be seen, the peptic activity of the gastric mucosa rose from 9. to 14.5 mm, a fact testifying that pepsin in the mucosa had more than doubled. This also produced an increase in solid residue and chlorides within the gastric mucosa.

Similar data were obtained when another type of nervous stimulus of the gastric glands was employed. Table 3 shows the changes in the composition of the gastric mucosa due to a natural conditioned reflex: the sight and smell of food.

It is evident from these records that conditioned reflex excitation of the gastric glands led to a build-up of pepsin, solids, and chlorides in the gastric mucosa.

Increase in the content of these substances in the gastric mucosa, due to nervous excitation, is proof of the positive effect of the central nervous system on trophic processes in the gastric glands.

The effect of the vagus nerve, as demonstrated in studies by our associates (Z. V. Dovgan', 1954, and L. N. Karpenko, 1954), is accompanied by excretion in the gastric juice of a parasympathetic mediator. Whether it is the effect of impulses from the vagus nerve, or whether the accumulation of blood acetylcholine is due to other reasons, a gastric secretion of high peptic activity and elevated solid residue (due to the increase in the amount of organic matter) occurs.

TABLE 2

EXPERIMENT OF 26 MAY 1954, DOG BURKA, 15 kg

| Time | Stimulus | Latent period, minutes | Juice secreted, quantity | Peptic activity of juice, (mm) | Chlorides, quantity | Residual solids (%) | Residual ash (%) | Organic residue (%) |
|---|---|---|---|---|---|---|---|---|
| 1340 | Mucosa, induction current to vagus nerve | | | 9.5 | 505.8 | 16.8 | 1.3 | 15.5 |
| 1408 | 30 minutes | 3 | 1.5 | 1.6 | 419.5 | | | |
| 1410 | Mucosa | | | 14.5 | 574.6 | 18.1 | 1.4 | 16.7 |
| 1420 | | | 1.5 | 3.4 | 455.0 | | | |
| 1430 | | | 0.8 | 4.0 | 437.25 | | | |

TABLE 3

EXPERIMENT OF 24 MAY 1954, DOG SURKA, 15 kg

| Time | Stimulus | Latent period, minutes | Juice secreted, quantity | Peptic activity of juice, (mm) | Chlorides, quantity | Residual solids (%) | Residual ash (%) | Organic residue (%) |
|---|---|---|---|---|---|---|---|---|
| 0942 | Mucosa, sight, and smell of food | | | 10.5 | 366.2 | 15.6 | 1.2 | 14.4 |
| 1000 | | 2 | 50.0 cloudy greenish liquid | 3.4 | 313.0 | | | |
| 1002 | Mucosa | | | 11.0 | 415.5 | 15.8 | 1.5 | 14.3 |
| 1012 | Mucosa | | | 12.5 | 485.6 | 16.3 | 1.4 | 14.9 |

We attained an increase in acetylcholine in the organism by subcutaneous introduction of physostigmine. When this was done, we observed an increase in secretion of gastric juice, and change in the composition of the gastric mucosa. Table 4 presents the corresponding data.

TABLE 4

EXPERIMENT OF 20 OCTOBER 1954, DOG VIKHR', 18.5 kg

| Time | Stimulus | Latent period, minutes | Juice secreted quantity | Peptic activity of juice (mm) | Chlorides, quantity | Residual solids (%) | Residual ash (%) | Organic residue (%) |
|---|---|---|---|---|---|---|---|---|
| [1] | [2] | [3] | [4] | [5] | [6] | [7] | [8] | [9] |
| | Mucosa | | | 12.0 | 473.3 | 20.4 | 1.6 | 18.8 |
| 1100 | Physostigmine (1:1000) - 1.7 | | | | | | | |
| 1125 | | 8 | 5.5 | 4.2 | 432.5 | 2.4 | 0.5 | 1.9 |
| 1140 | | | 9.5 | 4.6 | 426.0 | 2.4 | 0.6 | 1.8 |
| | Mucosa | | | 13.25 | 426.0 | 20.8 | 1.5 | 19.3 |

| [1] | [2] | [3] | [4] | [5] | [6] | [7] | [8] | [9] |
|---|---|---|---|---|---|---|---|---|
| 1155 | | | 7.0 | 4.6 | [illegible] | 2.3 | 1.6 | [illegible] |
| 1210 | | | 10.0 | 4.8 | 432.5 | | | |
| 1225 | | | 10.0 | 5.6 | 432.5 | | | |
| 1240 | | | 6.0 | 4.0 | 432.0 | | | |
| 1255 | | | 8.0 | 4.4 | 462.5 | | | |
| 1310 | | | 6.5 | 4.2 | 462.0 | | | |
| 1325 | | | 7.0 | 4.0 | 426.0 | | | |
| 1340 | | | 2.5 | 4.0 | 426.0 | | | |
| 1355 | | | 1.0 | - | - | | | |
| | Mucosa | | | 15.0 | 473.3 | 21.0 | 1.5 | 19.5 |

Without touching on the question as to the composition of the gastric juice, which was very similar to that resulting from nerve stimulus of the gastric glands, we turn our attention to chemical changes in the gastric mucosa. As can be seen from the data presented, the accumulation of blood acetylcholine stimulates gastric secretion, and leads to a considerable rise in the peptic activity of the gastric mucosa. There is some increase in the solid residue of the juice, only the chloride content remaining unchanged.

Thus, acetylcholine is a factor facilitating strengthening of the processes of recovery, exciting the secretory function of the stomach glands, and markedly increasing the trophics of glandular tissue.

In summarizing the data set forth above, we call attention to the fact that penetration into the intimate mechanisms of the process of secretion provides results that have both theoretical and practical importance.

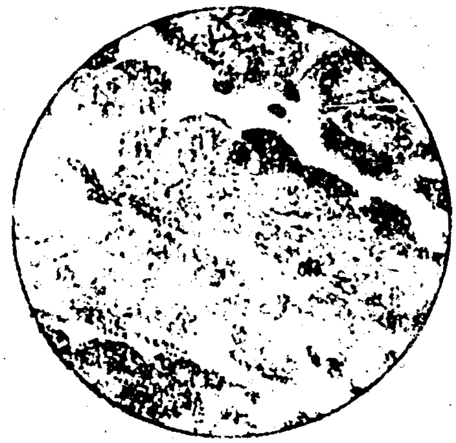

Figure 1. Gastric mucosa before secretion, magnified 1,000 times. Dominici-Kedrovskiy stain (microphoto).

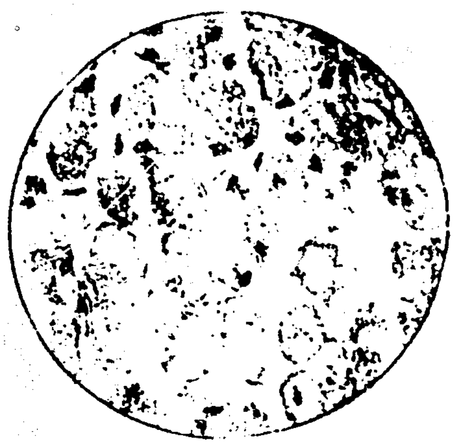

Figure 2. Gastric mucosa after long-term secretion. Magnified 1,000 times. Dominici-Kedrovskiy stain (microphoto).